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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/640,787	08/18/2000	Brendan Larder	07691.0005	7344

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EXAMINER	
WINKLER, ULRÍKE	

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/640,787	LARDER ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed May 28, 2002 (Paper No. 9) in response to the Office Action of February 27, 2002 is acknowledged and has been entered. Claims 1-20 are pending and claims 1-9 are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in European Patent Office on April 20, 2000. It is noted, however, that applicant has not filed a certified copy of the EPO 00201433.0 application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 12, is attached to the instant Office action, note that those references cited on prior IDS forms have been lined through.

Claim Rejections - 35 USC § 112

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **maintained.** Applicant cites to specific section in the specification, it is noted these replacement primes are to be used when the original sequencing primers "fail. It is not

clear what determines "failure". Furthermore, the specification states that in principle any described primer that covers the same sequence of the region SEQ2FOR can be used. Therefore, the metes and bounds of a replacement primer are unclear as it can be interpreted that any primer that allows for the sequencing of the amplified product will read on the term replacement primer.

The rejection of claims 1, 2, 5, 6 and 7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of the amendments to the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Hertogs et al. (Antiviral Agents and Chemotherapy, 1998, IDS paper No. 3) in view of any one of Zazzi et al (Molecular Biotechnology, 1998, paper No. 3), Kozal et al. (U.S.Pat No. 5,856,086), Birk et al. (Aids, 1998), Cabana et al. (Journal of Medical Virology, 1999) or Boden et al. (Journal of the American Medical Association, 1999) **is maintained** for reasons of record. Applicant arguments are that the office has not established a *prima facie* case according to MPEP §2143.

> MPEP §2143: To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)

Applicant argues that the specific primers of SEQ ID NO 3-12 are not taught in the prior art are and therefore the office cannot rely on the functional equivalents to support an obvious rejection. Applicant also argues the instant invention will sequence larger portions of the amplified product. These arguments are not found convincing since the reference of Hertog et al. teaches a sequencing product using a nested PCR method with outer primers SEQ ID NO 1 and 2 (OUT3-PRTO5), and a secondary primer pair (IN3-IN5). This amplification product comprises the sequences disclosed in SEQ ID 3-12. The reference additionally teaches the sequencing of the amplified PCR products (see table 1 and table 6). Therefore, the Hertog et al. reference by virtue of amplifying the nucleic acid product with the same outer primers (SEQ ID 1 and 2) as those disclosed in the instantly claimed invention, directs the ordinary artisan to a specific finite nucleic acid sequence for the purpose of determining the sequence phenotype. This is the sequence between the two outer primer pair. Therefore, following *In re Baird* (CA FC, 29 USPQ2d 1550) the Hetrzog et al. reference teaches a product having a finite sequence, additionally this product contains the nucleotide sequences set out in SEQ ID 3-12. Because the primers of SEQ ID 3-12 are found within a defined sequence this renders the primers obvious in view of the cited references.

Although the specific sequences of SEQ ID NO: 3-21 have not been disclosed in the prior art for the same purpose, the sequences that are disclosed in the prior art are functional equivalents of the instant sequences. The MPEP 2144.06 provides that in order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118

USPQ 340 (CCPA 1958). The specification does not provide the supporting rational for the obviousness rejection. Here the equivalence is related to the end product which is the determination of mutations in the *pol* gene, although the prior art does not teach the specific primers disclosed in SEQ ID Nos: 3-12, one having ordinary skill in the art would have already been directed to the 2.2 kilo base product from the outer primers disclosed by Hertzog et al. Zazzi et al. indicate that sequencing of this region is necessary for the determination of mutation in the *pol* region. In addition, the other cited references provide ample primers that detect smaller regions within the 2.2 kilo base product, all of which would produce the equivalent result of sequencing the regions associated with high mutation rates. If applicant's specific sequences produce an unexpected result, applicant needs to point out what those results are.

Therefore, the instant invention is rejected over Hertogs et al. in view of any one of Zazzi et al., Kozal et al., Birk et al., Cabana et al. or Boden et al.

Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hertogs et al. (Antiviral Agents and Chemotherapy, 1998, IDS paper No. 3) in view of Demeter et al. (Journal of Virological Methods, 1998, IDS #3).

Applicant argues that the specific primers of SEQ ID NO 3-12 are not taught in the prior art are and therefore the office cannot rely on the functional equivalents to support an obvious rejection. Applicant also argues the instant invention will sequence larger portions of the amplified product. These arguments are not found convincing since the reference of Hertog et al. teaches a sequencing product using nested PCR method with outer primers SEQ ID NO 1 and 2 (OUT3-PRTO5), and a secondary primer pair (IN3-IN5). This amplification product comprises

the sequences disclosed in SEQ ID 3-12. The reference additionally teaches the sequencing of the amplified PCR products (see table 1 and table 6). Therefore, the Hertog et al. reference by virtue of amplifying the nucleic acid product with the same outer primers (SEQ ID 1 and 2) as those disclosed in the instantly claimed invention, directs the ordinary artisan to a specific finite nucleic acid sequence for the purpose of determining the sequence phenotype. This is the sequence between the two outer primer pair. Therefore, following *In re Baird* (CA FC, 29 USPQ2d 1550) the Hetrzog et al. reference teaches a product having a finite sequence, additionally this product contains the nucleotide sequences set out in SEQ ID 3-12. Because the primers of SEQ ID 3-12 are found within a defined sequence this renders the primers obvious in view of the cited references.

Demeter et al. teaches using PCR to determine mutations in the HIV *pol* region and directly sequencing the PCR products (see sequencing methods). The reference teaches numerous primers that may be utilized for the original PCR step and the subsequent sequencing step.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize PCR in order to determine mutations in the *pol* gene of HIV-1 infected individuals. One having ordinary skill in the art would have been motivated to utilize a single PCR product for sequencing purposes in order to reduce the steps in the laboratory procedures. The advantage of the Hertog et al. primer is that it amplifies a large region of the HIV-1 gene, covering more areas affected by mutations in response to drug treatment. The choice of sequencing primer will determine which area of the gene is analyzed. Detemer et al. teach numerous primers which can be used to amplify or sequence different regions of *pol* gene

associated with drug resistance. Once the gene has been amplified the sequences can be analyzed by using different primers. The ordinary artisan would be motivated to detect viral mutation early in order to adjust treatment protocols before allowing the emerging viruses to replicate to great numbers. Due to the multiple mutations that are associated with drug resistance, multiple analysis of single *pol* codons is not feasible, thus sequencing the *pol* region which contain the potential drug resistance mutations is the only method allowing proper estimation of *in vivo* drug susceptibility based on the analysis of the viral genotype.

Therefore, the instant invention is rejected over Hertogs et al. in view of Demeter et al.

New rejections necessitated by Applicant's amendment:

Claim Rejections - 35 USC § 112

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to claim 1 wherein the outer primer is **chosen from** SEQ ID NO 1 **or** SEQ ID NO 2 is not supported by the specification. The method disclosed in the specification requires that the outer primer reaction be done as described in WO97/27480 which requires both primers. Therefore, there is lack of written description for using only a single outer primer.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D.

James C. Housel 8/9/02

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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